REMARKS

Claims 1, 3, 4 and 9-14 are pending in this application. Claims 11-14 have been withdrawn from consideration. By this Amendment, claims 1 and 10 are amended to define the presently claimed subject matter. Withdrawn claims 11-14 are amended for consistency. No new matter is added by this Amendment.

I. Rejection Under 35 U.S.C. §103(a)

The Office Action rejected claims 1, 3, 4, 9 and 10 under 35 U.S.C. §103(a) as allegedly being unpatentable over Van Rossum, et al., Review Article: Glycyrrhizin As A Potential Treatment For Chronic Hepatitis C, Aliment Pharmacol. Theor., Vol. 12, pages 199-205 (1998) ("Van Rossum") in view of U.S. Patent Application Publication No. 2002/0147201 ("Chen").

The Patent Office alleges that Van Rossum discloses administering a glycyrrhizin solution, referred to as Stronger Neo Minophagen C ("SNMC"), to patients. See Van Rossum, page 203, column 1, Clinical Investigations, first paragraph. However, the Patent Office admits that Van Rossum fails to disclose the glycyrrhizin, cysteine and aminoacetic acid concentrations and the absence of sulfite recited in claims 1 and 10. See Office Action, page 5, lines 14-19. The Patent Office thus introduces Chen as allegedly remedying the deficiencies of Van Rossum.

A. "Consisting Essentially Of"

Applicants submit that the cited references do not describe all of the limitations of amended independent claims 1 and 10. Specifically, the cited references do not teach or suggest (1) an injectable pharmaceutical composition consisting essentially of 8 to 16 mg/mL of glycyrrhizin, 3 to 6 mg/mL of cysteine and 80 to 160 mg/mL of aminoacetic acid, wherein substantially no sulfite is contained in the pharmaceutical composition, and wherein the glycyrrhizin, cysteine and aminoacetic acid are dissolved in water or (2) an injectable

pharmaceutical composition consisting essentially of 8 to 16 mg/mL (as glycyrrhizin) of monoammonium glycyrrhizinate, 4 to 8 mg/mL of cysteine hydrochloride and 80 to 160 mg/mL of aminoacetic acid, wherein substantially no sulfite is contained in the pharmaceutical composition, and wherein the monoammonium glycyrrhizinate, cysteine and aminoacetic acid are dissolved in water.

The courts have held that the transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials recited therein and exclude those materials that do not "materially affect the basic and novel characteristic(s)". See MPEP 2111.03 citing (*In re Herz*, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976) (emphasis in original)).

Van Rossum describes that SNML comprises glycyrrhizin, cysteine and aminoacetic acid dissolved in a physiological saline solution (i.e., salt and water). See Van Rossum, page 203, right column, lines 27-30. Furthermore, as compared to being dissolved in solely water, the osmotic pressure ratio of Van Rossum's composition (SNMC) containing salt water increases by about 1. The higher the osmotic pressure ratio of a drug, the more severely the drug results in an injurious effect to tissue.

As such, dissolving the components recited in claims 1 and 10 in the solvent of Van Rossum (i.e., a physiological saline solution) materially affects the recited pharmaceutical composition by increasing the osmotic pressure to such an extent that the composition injures tissue and is no longer suitable for its intended purpose.

The Patent Office introduces Chen as allegedly remedying the deficiencies of Van Rossum. Applicants submit that Chen, like Van Rossum, also does not describe an injectable pharmaceutical composition consisting essentially of the materials in the recited amounts, wherein substantially no sulfite is contained in the pharmaceutical composition, and wherein the monoammonium glycyrrhizinate, cysteine and aminoacetic acid are dissolved in water, as recited in claims 1 and 10.

Chen at best merely describes increasing the concentration of glycyrrhizin complexed with an active agent, not glycyrrhizin as a pharmaceutical agent in its own right. For this reason, Chen specifically defines "active agent" differently than "glycyrrhizin." See Chen, paragraphs [0021], [0031] and [0049]. As such, the glycyrrhizin referred to in Chen has no intended pharmacological use as Chen specifies that the active agent (i.e., famotidine) reverses complexes from the glycyrrhizin at a low pH and thus eventually forms a protonated active ingredient that more easily dissociates in the stomach. See Chen, paragraph [0053]. Because Chen describes a composition having glycyrrhizin as an additive to a composition that includes an "active agent" (i.e., glycyrrhizin complexed with an active agent), the active agents described in Chen would materially affect the basic and novel characteristics of the recited pharmaceutical compositions and thus be excluded from the recited claims.

Furthermore, even if one having ordinary skill in the art would have combined the disclosures of Van Rossum and Chen and increased the concentration of the components recited in Van Rossum, such a combination would not have resulted in the pharmaceutical compositions recited claims 1 and 10 because the combined composition would have included a physiological saline solution. For the reasons discussed above regarding Van Rossum, the physiological saline solution materially affects the recited pharmaceutical composition, and is thus excluded from claim 1 and 10.

Thus, Chen would have merely provided one having ordinary skill in the art would with a reason or rationale to have increased the concentration of a different glycyrrhizin compound (i.e., glycyrrhizin complexed with an active agent) and not glycyrrhizin as a pharmaceutical agent in its own right.

B. Unexpected Results Regarding No Sulfite

In the Amendment After Final Rejection ("AAFR"), filed July 30, 2010, Applicants argued that Van Rossum, alone or in combination with Chen, does not describe that a pharmaceutical composition comprised of glycyrrhizin, cysteine and aminoacetic acid in the recited concentration and including substantially no sulfite unexpectedly results in a pharmaceutical composition with improved stability and no glycyrrhizin precipitates. Applicants further provided evidence of this in the AAFR.

In response, the Patent Office alleged that the evidence was not commensurate with the scope of the present claims because claim 1 (and claim 10) only requires "substantially no sulfite" and the term "containing" in claim 1 is an open transitional phrase that does not exclude the presence of additional preservatives, such as those described in Chen.

However, as discussed above, Applicants have amended claims 1 and 10 to recite the transitional phrase "consisting essentially of", which effectively excludes those materials, such as the sulfites of Chen, that "materially affect the basic and novel characteristic(s)" of the pharmaceutical compositions recited in claims 1 and 10. Although the Patent Office notes that Chen discloses both sulfites and other preservatives (see Chen, paragraph [0059]), Chen discloses that sulfites are perfectly acceptable additives in the composition described therein. However, as further described by the evidence in the specification, the presence of sulfite decreases stability and forms glycyrrhizin precipitates, and thus materially affect the basic and novel characteristics of the recited compositions.

Although described in the AAFR, for the sake of completeness, the evidence in the specification is repeated herein. Specifically, the evidence consists of two sets of experiments (Experiment 1 and Experiment 2) that were used to determine the influence of sulfite on a pharmaceutical composition comprised of glycyrrhizin, cysteine and aminoacetic acid. The details for the preparation of the solutions of Experiment 1 (Solution 1 and Comparative

Solutions 1-2) and Experiment 2 (Solution 2 and Comparative Solution 3) are described at pages 6-8 of the present specification.

As shown below in Tables 1 and 2 (and Tables 1 and 2 of the original specification), the greater the concentration of sodium sulfite, the more the amount of cysteine is reduced as time passes. Furthermore, adding sodium sulfite precipitates the glycyrrhizin. However, in the cases where no sodium sulfite was added, glycyrrhizin did not precipitate and the amount of cysteine was not significantly reduced, which thus results in an improved stability of the pharmaceutical composition.

Table 1: Experiment 1

			Adding amount of sodium sulfite (mg/mL)		
			Solution 1	Comp. Solution 1	Comp. Solution 2
			0	2.4	4.0
pH at manufacturing			7.22	7.49	7.29
Presence or absence of precipitation of glycyrrhizin	After 4 years at 25°C		-	+	+
Amount of cysteine hydrochloride(%)	Before sterilization		97.3	101.6	98.9
	After sterilization		94.4	95.2	91.1
	60 °C	After 3 days	89.7	87.8	81.4
		After 7 days	81.2	71.3	64.2
		After 14 days	77.8	66.5	53.9
	40 °C	After 2 months	89.4	86.0	70.3
		After 4 months	83.6	77.7	68.5

Table 2: Experiment 2

	Concentration of cysteine hydrochloride (mg/mL)		8	6	4
Solution 2 (Non-addition of Sulfite)	Amount of cysteine hydrochloride (%)	Initial	100.0	100.0	100.0
		4 days	93.5	97.5	94.3
		7 days	88.6	94.5	89.5
		14 days	82.8	82.4	88.7
Comp. Solution 3 (Addition of Sulfite)	Amount of cysteine hydrochloride (%)	Initial	100.0	100.0	100.0
		4 days	73.6	84.4	88.8
		7 days	53.1	70.4	77.1
		14 days	40.4	52.2	59.8

In view of the above evidence, Applicants respectfully submit that the absence of sulfites unexpectedly results in a pharmaceutical composition with improved stability and no glycyrrhizin precipitates.

Furthermore, page 2 of the present specification describes that sulfites are conventionally added to compositions comprising glycyrrhizin, cysteine and aminoacetic acid in order to increase stability, i.e. decrease precipitation and degradation. In this way, a person of ordinary skill in the art would not have expected to increase stability by lessening the amount of a stabilizer, much less by omitting it altogether.

Therefore, the Applicants have demonstrated highly unexpected results by showing that stability can be increased by not including a compound that was known and conventionally used to increase stability. Instead, such a compound materially affects the basic and novel characteristics of the compositions recited in claims 1 and 10.

Withdrawal of the rejection is requested.

II. Rejoinder

Applicants respectfully submit that claims 1, 3, 4, 9 and 10 are in a condition for allowance for at least the reasons discussed above, and therefore Applicants respectfully submit that rejoinder and consideration of withdrawn claims 11-14 is proper. MPEP §821.04

states that claims eligible for rejoinder must depend from or require all the limitations of an allowable claim. Applicants suggest that claims 11-14, drawn to methods of treating hepatic diseases or methods of treating allergy require all the limitations of independent claim 1, and therefore are eligible for rejoinder under MPEP §821.04. Accordingly, rejoinder of claims 11-14 is respectfully requested.

III. Conclusion

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance. Favorable reconsideration and prompt allowance of claims 1, 3, 4 and 9-14 are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

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